Listing of claims:

For the convenience of the Examiner, all claims being examined are presented below.

30. **(Currently Amended)** A method to identify or characterize an inhibitor of IgG protection by human FcRn (huFcRn) comprising:

a) providing an muFcRn -/-, +huFcRn transgenic mouse;

b) administering tracer human IgG and tracer human IgA to the mouse;

c) administering a candidate inhibitor to the mouse; and

d) determining the half-life of the tracer human IgG and tracer human IgA in the mouse which has received the candidate inhibitor as compared to the half-life of administered tracer human IgG and tracer human IgA in a muFcRn -/-, +huFcRn transgenic mouse which has not received inhibitor, with a decrease in the half-life of the tracer human IgG, but not the tracer human IgA, in the mouse which has received candidate inhibitor, as compared to the half life of the tracer human IgG and tracer human IgA respectively in the mouse which has not received candidate inhibitor, being an indication that the candidate inhibitor inhibits FcRn protection of IgG.

47. **(Currently Amended)** A method to identify or characterize a candidate agent for FcRn-mediated drug delivery, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug delivery attached to a trackable composition;

b) administering the formulation to a muFcRn-/-, +huFcRn transgenic knockout mouse, and also to a muFcRn-/- transgenic knockout mouse; and

c) assaying the muFcRn-/-, +huFcRn transgenic knockout mouse and the muFcRn-/- transgenic knockout mouse for presence of the formulation in the bloodstream, with a substantially higher amount of the formulation in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse as compared to the amount of the formulation in the bloodstream of the muFcRn-/- transgenic knockout mouse being an indication that the candidate agent facilitates FcRn-mediated drug delivery.

48. **(Original)** The method of Claim 47 wherein the candidate agent is derived from an immunoglobulin Fc region.

49. **(Currently Amended)** The method of Claim 47 wherein the candidate agent is derived from an FcRn binding partner.

50. **(Original)** The method of Claim 47 wherein the candidate agent is transported via the FcRn through the intestinal epithelium, mucosal epithelium, epithelium of the lung or transdermally.

51. **(Original)** The method of Claim 47 wherein the candidate agent is administered orally, as an aerosol, to pulmonary or nasal epithelial mucosal tissue, or transdermally.

52. **(Currently Amended)** A method to identify or characterize a candidate agent for FcRn-mediated drug delivery in the fetus or neonate, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug delivery attached to a trackable composition;

b) administering the formulation to either a neonate or pregnant muFcRn -/-, +huFcRn transgenic knockout mouse, and also to either a neonate or pregnant muFcRn -/- knockout mouse; and

c) assaying both the neonatal or fetal muFcRn -/-, +huFcRn and muFcRn -/- transgenic knockout mice for presence of the formulation in the bloodstream, with a substantially higher amount of the formulation in the bloodstream of the neonatal or fetal muFcRn -/-, +huFcRn transgenic knockout mouse as compared to the amount of the formulation in the bloodstream of the neonatal or fetal muFcRn -/- transgenic knockout mouse being an indication that the candidate agent facilitates FcRn-mediated drug delivery.

53. **(Original)** The method of Claim 52 wherein the candidate agent is derived from an immunoglobulin Fc region.

54. **(Currently Amended)** The method of Claim 52 wherein the candidate agent is derived from an FcRn binding partner.

55. **(Original)** The method of Claim 52 wherein the candidate agent is transported via FcRn through the intestinal epithelium, mucosal epithelium, epithelium of the lung or transdermally.

56. **(Original)** The method of Claim 52 wherein the candidate agent is administered orally, as an aerosol, to pulmonary or nasal epithelial mucosal tissue, or transdermally.

57. **(Original)** A method to identify or characterize a candidate agent for FcRn-mediated drug stabilization, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug stability attached to a trackable composition;

b) administering the formulation to a muFcRn-/-, +huFcRn transgenic knockout mouse, and also to a muFcRn-/- transgenic knockout mouse; and

c) assaying the half-life of the formulation in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse and the bloodstream of the muFcRn-/- transgenic knockout mouse, with a substantially longer half-life in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse being an indication that the candidate agent promotes FcRn-mediated drug stabilization.

58. **(Original)** The method of Claim 57 wherein the candidate agent is derived from an immunoglobulin Fc region.

59. **(Original)**The method of Claim 57 wherein the candidate agent is derived from an Fc region or fragment thereof, or other molecules which are structurally-similar or similar in sequence identity to the Fc-region of IgG.

60. **(Currently Amended)** The method of Claim 57 wherein the candidate agent is structurally-similar or similar in sequence identity to the Fc-region of IgG, such that the binding affinity of the candidate agent to the FcRn protein is greater than the binding affinity of the Fc-region of IgG to the FcRn protein.

61. **(Currently Amended)** A method for determining the difference in pharmacokinetics of a drug conferred by an FcRn-mediated drug stability candidate agent linked to the drug, comprising:

a) providing a first trackable formulation comprising a drug linked to a FcRn-mediated drug stability candidate agent, and a second trackable formulation comprising the drug without the FcRn-mediated drug stability candidate agent;

b) administering the first formulation to a first muFcRn-/-, +huFcRn transgenic knockout mouse, and the second formulation to a second muFcRn-/-, +huFcRn transgenic knockout mouse;

c) determining the half-lives of the first and the second formulation in the bloodstream of the first and the second muFcRn-/-, +huFcRn transgenic knockout mouse respectively; and

d) comparing the half-lives determined in step c) to one another, thereby determining the difference in half-lives conferred to the drug by the FcRn-mediated drug stability candidate agent.

62. **(Original)** The method of Claim 61 wherein the candidate agent is derived from an immunoglobulin Fc region.

63. **(Original)** The method of Claim 61 wherein the candidate agent is derived from an Fc region or fragment thereof, or other molecules which are structurally-similar or similar in sequence identity to the Fc-region of IgG.

64. **(Currently Amended)** The method of Claim 61 wherein the candidate agent is structurally-similar or similar in sequence identity to the Fc-region of IgG, such that the binding affinity of the candidate agent to the FcRn protein is greater than the binding affinity of the Fc-region of IgG to the FcRn protein.

Please add the following new claims:

81. **(New)** The method of claim 49, wherein the FcRn binding partner is an immunoglobulin or a portion thereof.

82. **(New)** The method of claim 54, wherein the FcRn binding partner is an immunoglobulin or a portion thereof.

83. **(New)** A method to identify or characterize a candidate agent for FcRn-mediated drug delivery, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug delivery formulated with a trackable composition;

b) administering the formulation to a muFcRn-/-, +huFcRn transgenic knockout mouse, and also to a muFcRn-/- transgenic knockout mouse; and

c) assaying the muFcRn-/-, +huFcRn transgenic knockout mouse and the muFcRn-/- transgenic knockout mouse for presence of the formulation in the bloodstream, with a substantially higher amount of the formulation in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse as compared to the amount of the formulation in the bloodstream of the muFcRn-/- transgenic knockout mouse being an indication that the candidate agent facilitates FcRn-mediated drug delivery.

84. **(New)** A method to identify or characterize a candidate agent for FcRn-mediated drug delivery in the fetus or neonate, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug delivery formulated with a trackable composition;

b) administering the formulation to either a neonate or pregnant muFcRn -/-, +huFcRn transgenic knockout mouse, and also to either a neonate or pregnant muFcRn -/- knockout mouse; and

c) assaying both the neonatal or fetal muFcRn -/-, +huFcRn and muFcRn -/- transgenic knockout mice for presence of the formulation in the bloodstream, with a substantially higher amount of the formulation in the bloodstream of the neonatal or fetal muFcRn -/-, +huFcRn transgenic knockout mouse as compared to the amount of the formulation in the bloodstream of the neonatal or fetal muFcRn -/- transgenic knockout mouse being an indication that the candidate agent facilitates FcRn-mediated drug delivery.

85. **(New)** A method to identify or characterize a candidate agent for FcRn-mediated drug stabilization, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug stability formulated with a trackable composition;

b) administering the formulation to a muFcRn-/-, +huFcRn transgenic knockout mouse, and also to a muFcRn-/- transgenic knockout mouse; and

c) assaying the half-life of the formulation in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse and the bloodstream of the muFcRn-/- transgenic knockout mouse, with a substantially longer half-life in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse being an indication that the candidate agent promotes FcRn-mediated drug stabilization.

86. **(New)** A method for determining the difference in pharmacokinetics of a drug conferred by an FcRn-mediated drug stability candidate agent linked to the drug, comprising:

a) providing a first trackable formulation comprising a drug linked to a FcRn-mediated drug stability candidate agent, and a second trackable formulation comprising the drug without the FcRn-mediated drug stability candidate agent;

b) administering the first and the second formulation to a muFcRn-/-, +huFcRn transgenic knockout mouse;

c) determining the half-lives of the first and the second formulation in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse; and

e) comparing the half-lives determined in step c) to one another, thereby determining the difference in half-lives conferred to the drug by the FcRn-mediated drug stability candidate agent.

The amended claims are restated below to reflect changes to the claims as filed.

30. **(Currently Amended)** A method to identify or characterize an inhibitor of IgG protection by <u>human FcRn (</u>huFcRn<u>)</u> comprising:

a) providing an <u>mu</u>FcRn -/-, +huFcRn transgenic mouse;

b) administering tracer human IgG and tracer human IgA to the mouse;

c) administering a candidate inhibitor to the mouse; and

d) determining the half-life of the tracer human IgG and tracer human IgA in the mouse which has received the candidate inhibitor as compared to the half-life of administered tracer human IgG and tracer human IgA in a muFcRn -/-, +huFcRn transgenic mouse which has not received inhibitor, with a decrease in the half-life of the tracer human IgG, but not the tracer human IgA, in the mouse which has received candidate inhibitor, as compared to the half ~~lives~~ life of the tracer human IgG and tracer human IgA respectively in the mouse which has not received candidate inhibitor, being an indication that the candidate inhibitor inhibits FcRn protection of IgG.

47. **(Currently Amended)** A method to identify or characterize a candidate agent for FcRn-mediated drug delivery, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug delivery attached to a trackable composition;

b) administering the formulation to a muFcRn-/-, +huFcRn transgenic knockout mouse, and also to a muFcRn-/- transgenic knockout mouse; and

c) assaying the muFcRn-/-, +huFcRn transgenic knockout mouse and the muFcRn-/- transgenic knockout mouse for presence of the formulation in the bloodstream, with a substantially higher amount of the formulation in the bloodstream of the muFcRn-/-, +huFcRn transgenic knockout mouse as compared to the amount of the formulation in the bloodstream of the muFcRn-/- transgenic knockout mouse being an indication that the candidate agent facilitates FcRn-mediated drug delivery.

49. **(Currently Amended)** The method of Claim 47 wherein the candidate agent is derived from an FcRn binding partner~~, such as immunoglobulins or portions thereof~~.

52. **(Currently Amended)** A method to identify or characterize a candidate agent for FcRn-mediated drug delivery in the fetus or neonate, comprising:

a) providing a formulation comprising a candidate agent for FcRn-mediated drug delivery attached to a trackable composition;

b) administering the formulation to ~~a~~ either a neonate or pregnant muFcRn -/-, +huFcRn transgenic knockout mouse, and also to either a neonate or pregnant muFcRn -/- knockout mouse; and

c) assaying both the neonatal or fetal muFcRn -/-, +huFcRn and muFcRn -/- transgenic knockout mice for presence of the formulation in the bloodstream, with a substantially higher amount of the formulation in the bloodstream of the neonatal or fetal muFcRn -/-, +huFcRn transgenic knockout mouse as compared to the amount of the formulation in the bloodstream of the neonatal or fetal muFcRn -/- transgenic knockout mouse being an indication that the candidate agent facilitates FcRn-mediated drug delivery.

54. **(Currently Amended)** The method of Claim 52 wherein the candidate agent is derived from an FcRn binding partner~~, such as immunoglobulins or portions thereof~~.

60. **(Currently Amended)** The method of Claim 57 wherein the candidate agent is structurally-similar or similar in sequence identity to the Fc-region of IgG, such that the ~~engineered molecule binds with greater affinity~~ binding affinity of the candidate agent to the FcRn protein is greater than the binding affinity of the Fc-region of IgG to the FcRn protein.

61. **(Currently Amended)** A method for determining the difference in pharmacokinetics of a~~n agent~~ drug ~~linked to~~ conferred by an FcRn-mediated drug stability candidate agent linked to the drug, comprising:

a) providing a first trackable formulation comprising ~~an agent~~ the drug linked to a ~~candidate agent for~~ FcRn-mediated drug stability candidate agent, and a second trackable formulation comprising the drug without the FcRn-mediated drug stability candidate agent;

b) administering the first formulation to a first muFcRn-/-, +huFcRn transgenic knockout mouse, and the second formulation to a second muFcRn-/-, +huFcRn transgenic knockout mouse;

c) determining the half-~~life~~ lives of the first and the second formulation in the bloodstream of the first and the second muFcRn-/-, +huFcRn transgenic

knockout mouse respectively; ~~as compared to the half-life of the agent, formulated without the candidate agent for FcRn-mediated drug stability~~; and

d) comparing the half-lives determined in step c) to one another, ~~to~~ thereby determineing the difference in half-life conferred to the ~~agent~~ drug by the ~~candidate agent for~~ FcRn mediated drug stability candidate agent.

64. **(Currently Amended)** The method of Claim 61 wherein the candidate agent is structurally-similar or similar in sequence identity to the Fc-region of IgG, such that the ~~engineered molecule binds with greater affinity~~ binding affinity of the candidate agent to the FcRn protein is greater than the binding affinity of the Fc-region of IgG to the FcRn protein.